

In the claims

Please cancel claims 1-16 and add new claims 17-79 as follows:

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17. (New) A polynucleotide in substantially isolated form comprising a contiguous

nucleotide sequence selected from the group consisting of:

- as
- (a) a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
 - (b) a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
 - (c) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII, and
 - (d) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII.

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18. (New) The polynucleotide according to claim 17, wherein said contiguous nucleotide sequence encodes a human antibody specific for factor VIII.

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19. (New) The polynucleotide according to claim 17, wherein said contiguous nucleotide sequence encodes a light chain of a human antibody specific for factor VIII.

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20. (New) The polynucleotide according to claim 17, wherein said contiguous nucleotide sequence encodes a heavy chain human antibody specific for factor VIII.
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21. (New) The polynucleotide according to claim 17, wherein said complementarity-determining region is a CDR3 region.
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22. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII is of a class selected from the group consisting of IgA, IgD, IgE, IgG and IgM.
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23. (New) The polynucleotide according to claim 22, wherein the human antibody specific for factor VIII is an IgG.
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24. (New) The polynucleotide according to claim 23, wherein the human antibody specific for factor VIII is an IgG from subclass IgG4.
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25. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII comprises an immunoglobulin chain selected from the group consisting of: an immunoglobulin heavy chain, an immunoglobulin light chain, a fragment of an immunoglobulin heavy chain and a fragment of an immunoglobulin light chain.
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26. (New) The polynucleotide according to claim 25, wherein the polynucleotide comprises a VH-gene segment.

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27. (New) The polynucleotide according to claim 26, wherein the VH-gene segment of the human antibody specific for factor VIII is derived from a VH-gene segment selected from the group consisting of: a segment derived from a DP-10 segment, a segment derived from a DP-14 segment, a segment derived from a DP-15 segment, a segment derived from a DP-31 segment, a segment derived from a DP-47 segment, a segment derived from a DP-49 segment and a segment derived from a DP-77 segment.

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28. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII is a single chain antibody.

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29. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII is specific for the heavy chain of factor VIII.

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30. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII is specific for the light chain of factor VIII.

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31. (New) The polynucleotide according to claim 29, wherein the human antibody factor VIII is specific for a domain of the heavy chain of factor VIII selected from the group consisting of the A1 domain, the A2 domain and the B domain.

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32. (New) The polynucleotide according to claim 30, wherein the human antibody is specific for a domain of the light chain of factor VIII selected from the group consisting of the A3 domain, the C1 domain and the C2 domain.

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33. (New) The polynucleotide according to claim 30, wherein the human antibody specific for the light chain of factor VIII is scFv-EL14.

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34. (New) The polynucleotide according to claim 30, wherein the human antibody specific for the light chain of factor VIII is scFv-IT2.

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35. (New) The polynucleotide according to claim 17, wherein the human antibody specific for factor VIII neutralizes the activity of factor VIII inhibitors of haemophilia A patients.

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36. (New) The polynucleotide according to claim 35, wherein the factor VIII inhibitors of haemophilia A patients are antibodies specific for factor VIII.

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37. (New) The polynucleotide according to claim 36, wherein the factor VIII inhibitors of haemophilia A patients are antibodies specific for the A2 domain, the A3 or the C2 domain of factor VIII.

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38. (New) The polynucleotide according to claim 37, wherein the human antibody specific for factor VIII that neutralizes the activity of factor VIII inhibitors shields the sites of factor VIII bound by the inhibitors.

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39. (New) The polynucleotide according to claim 38, wherein the human antibody specific for factor VIII that neutralizes the activity of factor VIII inhibitors and shields the sites of factor VIII bound by the inhibitors is specific for the A3-C1 domain or the A2 domain of factor VIII.

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40. (New) The polynucleotide according to claim 17, wherein the contiguous nucleotide sequence is at least about eight nucleotides in length.

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41. (New) The polynucleotide according to claim 40, wherein the contiguous nucleotide sequence is at least about ten nucleotides in length.

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42. (New) The polynucleotide according to claim 40, further comprising a detectable label.

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43. (New) The polynucleotide according to claim 42, wherein the detectable label is a radioactive atom, a radioactive group, an enzyme, a fluorescent group, a luminescent group, a dye or biotin.

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44. (New) A kit comprising a polynucleotide in substantially isolated form comprising a contiguous nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,

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- (b) a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
 - (c) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
 - (d) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII;
- wherein the kit further comprises a suitable container.

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45. (New) The kit according to claim 44, wherein the polynucleotide further comprises a detectable label.

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46. (New) The kit according to claim 45, wherein the detectable label is a radioactive atom, a radioactive group, an enzyme, a fluorescent group, a luminescent group, a dye or biotin.

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47. (New) The kit according to claim 44, comprising a first and a second polynucleotide; the first polynucleotide being a polynucleotide of (a) and the second polynucleotide being a polynucleotide of (b); or the first polynucleotide being a polynucleotide of (c) and the second polynucleotide being a polynucleotide of (d).

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48. (New) The kit according to claim 47, wherein the first and the second polynucleotides form a primer pair suitable for priming cDNA synthesis.

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49. (New) The kit according to claim 48, wherein the polynucleotide primer pair are each between about 20 nucleotides and about 36 nucleotides in length.

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50. (New) The kit according to claim 48, further comprising a polynucleotide probe comprising a contiguous nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
- (b) a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
- (c) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII, and
- (d) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII;

wherein the polynucleotide probe hybridizes to a nucleotide sequence that occurs between but does not include the first or second polynucleotides of the primer pair.

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51. (New) A method for detecting a nucleic acid encoding a human antibody specific for factor VIII, comprising:

- (i) providing a sample containing nucleic acids for testing,

(ii) contacting the sample with a polynucleotide probe under conditions suitable for selective hybridization of the polynucleotide probe with a complementary nucleotide sequence; wherein the polynucleotide probe comprises a contiguous nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
- (b) a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII,
- (c) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII, and
- (d) a nucleotide sequence that selectively hybridizes under stringent conditions to a nucleotide sequence complementary to a nucleotide sequence encoding a complementarity-determining region of a human antibody specific for factor VIII;

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(iii) determining whether the polynucleotide probe is hybridized to a complementary nucleotide sequence in the sample.

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~~52.~~ (New) The method according to claim 51, wherein the nucleic acids in the sample are amplified by polymerase chain reaction prior to step (ii) using a first and a second primer; wherein the first primer is a polynucleotide of (a) and the second primer is a polynucleotide of (b); or the first primer is a polynucleotide of (c) and the second primer

is a polynucleotide of (d); wherein the polynucleotide probe hybridizes to a nucleotide sequence that occurs between but does not include the polynucleotide of the first primer or of the second primer.

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53. (New) A polypeptide in substantially isolated form that specifically binds factor VIII, wherein the polypeptide comprises:

- (i) an amino acid sequence from a complementarity-determining region of a human antibody specific for factor VIII;
- (ii) an amino acid sequence that mimicks the factor VIII-binding of a complementarity-determining region of a human antibody specific for factor VIII; or
- (iii) a derivative of an amino acid sequence from a complementarity-determining region of a human antibody specific for factor VIII.

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54. (New) The polynucleotide according to claim 53, wherein said complementarity-determining region is a CDR3 region.

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55. (New) The polypeptide according to claim 53, wherein the amino acid sequence of the polypeptide comprises an amino acid sequence of at least about four contiguous amino acids from within an immunoglobulin heavy chain sequence or an immunoglobulin light chain sequence.

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~~56~~. (New) The polypeptide according to claim 55, wherein the amino acid sequence of at least about four contiguous amino acids from within the immunoglobulin heavy chain sequence or the immunoglobulin light chain sequence comprise a sequence of at least four contiguous amino acids from a variable region.

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~~57~~. (New) The polypeptide according to claim 56, wherein the variable region is a heavy chain variable region.

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~~58~~. (New) The polypeptide according to claim 57, wherein the heavy chain variable region is derived from one of the following: DP-10, DP-14, DP-15, DP-31, DP-47, DP-49 and DP-77.

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~~59~~. (New) The polypeptide according to claim 53, wherein the human antibody is of a class selected from the group consisting of IgA, IgD, IgE, IgG and IgM.

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~~60~~. (New) The polypeptide according to claim 59, wherein the human antibody is an IgG.

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~~61~~. (New) The polypeptide according to claim 60, wherein the human antibody is an IgG from subclass IgG4.

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~~62~~. (New) The polypeptide according to claim 53, wherein the human antibody is a single chain antibody.

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63. (New) The polypeptide according to claim 53, wherein the polypeptide specifically binds the heavy chain of factor VIII.

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64. (New) The polypeptide according to claim 53 wherein the polypeptide specifically binds the light chain of factor VIII.

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65. (New) The polypeptide according to claim 63, wherein human antibody specifically binds a domain of the heavy chain of factor VIII consisting of the A1 domain, the A2 domain and the B domain of factor VIII.

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66. (New) The polypeptide according to claim 64, wherein the polypeptide specifically binds a region of the light chain of factor VIII consisting of the A3 domain, the C1 domain and the C2 domain of factor VIII.

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67. (New) The polypeptide according to claim 66, wherein the polypeptide is the single chain antibody scFv-EL14.

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68. (New) The polypeptide according to claim 66, wherein the polypeptide is the single chain antibody scFv-IT2.

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69. (New) The polypeptide according to claim 53, wherein the polypeptide reduces the activity of factor VIII inhibitors of haemophilia A patients.

2128 77. (New) The polypeptide according to claim 69, wherein the factor VIII inhibitors of haemophilia A patients are antibodies specific for factor VIII.

78 78. (New) The polypeptide according to claim 70, wherein the factor VIII inhibitors of haemophilia A patients are antibodies specific for the A2 domain, the A3 domain or the C2 domain of factor VIII.

79 79. (New) The polypeptide according to claim 71, wherein the polypeptide that reduces the activity of factor VIII inhibitors of haemophilia A patients is specific for the A3-C1 domain or the A2 domain of factor VIII.

80 80. (New) A polypeptide in substantially isolated form comprising a polypeptide that specifically binds an antibody specific for factor VIII, wherein the polypeptide comprises:

- (i) an amino acid sequence from a complementarity-determining region of a human antibody;
- (ii) an amino acid sequence that mimicks the binding of a complementarity-determining region of a human antibody;
- (iii) a derivative of an amino acid sequence from a complementarity-determining region of a human antibody.

81 81. (New) A pharmaceutical composition for the treatment of factor VIII inhibition in a human individual, comprising: a polypeptide that specifically binds factor VIII, or a

polypeptide that specifically binds an antibody specific for factor VIII, wherein the polypeptide comprises:

- (i) an amino acid sequence from a complementarity-determining region of a human antibody;
- (ii) an amino acid sequence that mimicks the factor VIII-binding of a complementarity-determining region of a human antibody; or
- (iii) a derivative of an amino acid sequence from a complementarity-determining region of a human antibody;

in a pharmaceutically acceptable carrier.

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75. (New) The pharmaceutical composition of claim 74, further comprising factor VIII or a compound with factor VIII activity.

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76. (New) A method of treatment of factor VIII inhibition in a human individual, comprising administering a polypeptide that specifically binds factor VIII, or a polypeptide that specifically binds an antibody specific for factor VIII, wherein the polypeptide comprises:

- (i) an amino acid sequence from a complementarity-determining region of a human antibody;
- (ii) an amino acid sequence that mimicks the factor VIII-binding of a complementarity-determining region of a human antibody; or
- (iii) a derivative of an amino acid sequence from a complementarity-determining region of a human antibody.